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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,626	05/11/2005	Toren Finkel	4239-67020-02	8541

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
10/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,626	FINKEL ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16, 20-29 and 48-59* is/are pending in the application.

4a) Of the above claim(s) *20-29 and 51-53* is/are withdrawn from consideration.

5)☒ Claim(s) *48-50,58 and 59* is/are allowed.

6)☒ Claim(s) *1-16, 48-50 and 54-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 04/23/09 has been acknowledged and fully considered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claims 1-16, 20-29 and 48-59 are pending.

This application contains claims 20-29 and 51-53 are drawn to an invention nonelected with traverse in the reply filed on 08/14/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Note: Earlier applicant elected Group I claims 1-16 and 48-50 (08/14/07). Therefore, claims 1-16, 48-50 and 54-59 are examined in this office action, whereas claims 20-29 and 51-53 that represented Group III stand withdrawn from further consideration.

Claim Rejections - 35 USC § 103

Claims 1-16, 48-50 and 54-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vasa et al[A] (Circ. Res. 89(1):E1-7, 2001, ref. of record on PTO-1449), Vasa et al[B] (Circulation. 103(24):2885-90, 2001, ref. of record on PTO-1449) and Scott et al (Circulation. 104:491-496, 2001), for the reason of record as set forth in the office action mailed on 12/24/08.

Response to Argument

Regarding Vasa et al[A], the applicant argues that cited art does not describe any subpopulations or confirm any associations of EPC with risk in the healthy control subjects. Regarding Vasa et al[B] the applicant argues that the art does teach that there is an increased number of circulating EPCs in healthy subjects treated with Atorvastatin, but does not suggest, nor render obvious, that this increase is associated with

increased vascular function in healthy subjects without symptomatic cardiovascular disease, and thus does not provide any indication of which asymptomatic subjects have reduced risk for developing cardiovascular disease in the future. The applicant argues that in view of large amount of research indicated by Grundy to be required, it is difficult to determine why this publication can be seen to provide a reasonable expectation that any method would be effective that utilized the FHS results, let alone the claimed methods.

The applicant further argues that clinical markers of advanced disease, or of disease progression, cannot necessarily be used to determine which asymptomatic individuals are at risk for developing a disease in the future. The applicant argues that one of skill in the art would predict that a test that is of use for determining an outcome in subject with coronary artery disease would not be predictive for the outcome in asymptomatic individuals. The applicant argues that the scientific evidence in the prior art teaches away from the arbitrary conclusions asserted in the Office action.

However the applicant's arguments are found not persuasive. The scope of the vascular function as broadly claimed herein encompasses coronary artery disease (CAD). Vasa et al[A] clearly teaches number and migratory activity of circulating Endothelial Progenitor Cells (EPCs) inversely correlate with risk factors for coronary artery disease (CAD). Contrary to applicant's assertion, the cited art teaches the isolation and enumeration of EPCs from the peripheral blood of patients with coronary artery disease (CAD) and compared the results to a healthy control sample (see abstract, page 4, fig(s) 2-4). The applicant fails to consider that the cited art clearly teaches that CD34-/KDR-positive cells were significantly reduced by ~48% in patients with CAD compared with Nine (9) age-matched healthy volunteers (see Fig 4A). The cited art concluded that the number of risk factors was inversely correlated with the levels of CD34-/KDR-positive cells (page 3. col.2 para.2). Furthermore, the cited art clearly suggest that one may speculate that the impairment of circulating EPCs may contribute to an insufficient regeneration of the endothelium (i.e. arterial hyperplasia) , which may lead to endothelial dysfunction (i.e. vascular contractility) see page 6, col.1 para 1, table-1. In addition, Vasa et al[B] teaches increase in circulating EPCs by statin

therapy in patients with stable coronary artery disease (CAD) se page 2888 fig-3, fig-4. The cited clearly teaches the isolation and enumeration of EPCs from the peripheral blood of patients with coronary artery disease (CAD) and compared the results to a control sample (see page 2887, fig-2A). The applicant fails to consider that the increased number of EPCs was paralleled by an enhancement of the migratory capacity of isolated EPCs. Mobilization of circulating EPCs with enhanced functional activity might contribute to the well-established beneficial effects of statins in patients with CAD as it is well established that EPCs participate in repair after ischemic injury (page 2889, col.1 para. 2). The cited art further teaches that statin therapy has shown to rapidly enhance coronary blood flow in patients with stable CAD and to reduce myocardial ischemia after an acute ischemic episode within a few weeks of treatment (page 2889, col.2 para. 4). Thus in view of teaching that number and migratory activity of circulating EPCs inversely correlate with risk factors for CAD (a vascular disease), it would have been obvious to conclude that any asymptomatic individuals with lower number of EPCs individuals are at risk for developing a CAD in the future.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law (**See MPEP 2144**). In the instant case Vasa et al[A] and Vasa et al[B] clearly teaches that number and migratory activity of circulating Endothelial Progenitor Cells (EPCs) inversely correlate with risk factors for coronary artery disease (CAD), therefore provides a clear rationale that any increase in number of EPCs in healthy subject is associated with increased vascular function or visa versa. Thus there is a reasonable expectation of success in predicting a sate of vascular function (i.e. CAD) even in asymptomatic subjects even having low Framingham Risk Score especially in

view of prior art teaching that number and migratory activity of circulating EPCs inversely correlate with risk factors for CAD (vascular disease).

Thus it would have been obvious to one ordinary skilled in the art at the time the instant invention was made to modify the invention of Vasa et al[A] and Vasa et al[B] with Scott et al to include Framingham Risk Score factors equations. One would have been motivated to do so to because Framingham Risk Score has been historically used to in the variety of cardiovascular studies. One would have a reasonable expectation of success, since the use of Framingham Risk Score equations has been routine in the art and Vasa et al[A&B] clearly teaches number and migratory activity of circulating Endothelial Progenitor Cells (EPCs) inversely correlate with risk factors for coronary artery disease at time the instant invention was made. Thus all of the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one of ordinary skill in the art at the time of the invention (*See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, U.S. 2007). Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention because the number of EPCs is inversely correlate with risk factors for coronary artery disease which is considered as vascular function abnormality. Therefore the invention as claimed is prima facie obvious in view of cited prior art of record.

Conclusion

Claims 1-16, 48-50 and 54-57 are rejected.

Claims 48-50 and 58-59 are allowed.

Claims 20-29 and 51-53 that represented Group III stand withdrawn from further consideration as a result of a restriction requirement.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sumesh Kaushal/
Primary Examiner, Art Unit 1633

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